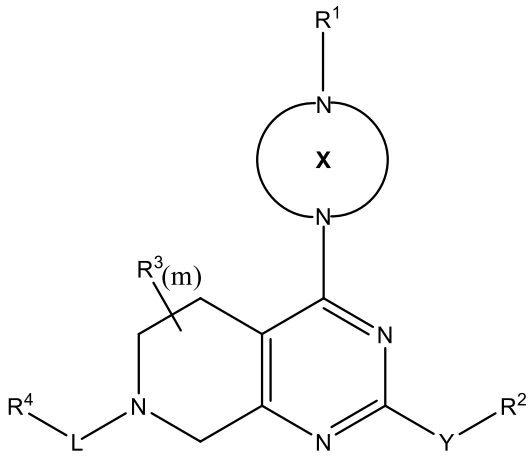
CLAIMS

WE CLAIM:

1. A compound of formula (II):



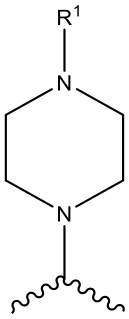
Formula (II)

or a pharmaceutically acceptable salt thereof:

wherein:

Y is a bond, O, S or NR^5;

R^1 is $-C(O)C(R^A)$ ====== $C(R^B)_p$, wherein ====== is a double bond, p is two, each R^B is hydrogen;

R^1-X is , wherein the piperazinyl ring is optionally substituted with R^8;

R^2 is hydrogen, alkyl, hydroxyalkyl, dihydroxyalkyl, alkylaminylalkyl, dialkylaminylalkyl, -Z-NR^5R^{10}, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, or heteroarylalkyl, wherein each of the Z, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, and heteroarylalkyl may be optionally substituted with one or more R^9;

each Z is C1 – C4 alkylene;

each R^3 is independently C1 – C3 alkyl, oxo, haloalkyl, hydroxyl or halogen;

L is a bond, -C(O)-, or C1 – C3 alkylene;

R^4 is hydrogen, cycloalkyl, heterocyclyl, aryl, aralkyl or heteroaryl, wherein each of the cycloalkyl, heterocyclyl, aryl, aralkyl and heteroaryl may be optionally substituted with one or more R^6, R^7 or R^8;

each R^5 is independently hydrogen or C1 – C3 alkyl;

R^6 is cycloalkyl, heterocyclyl, heterocyclylalkyl, aryl, or heteroaryl, wherein each of the cycloalkyl, heterocyclyl, aryl, or heteroaryl may be optionally substituted with one or more R^7;

each R^7 is independently halogen, hydroxyl, C1 – C6 alkyl, cycloalkyl, alkoxy, haloalkyl, amino, cyano, heteroalkyl, hydroxyalkyl or Q-haloalkyl, wherein Q is O or S;

R^8 is oxo, C1 – C3 alkyl, C2 – C4 alkynyl, heteroalkyl, cyano, $-C(O)OR^5$, $-C(O)N(R^5)_2$, $-N(R^5)_2$, wherein the C1 – C3 alkyl may be optionally substituted with cyano, halogen, $-OR^5$, $-N(R^5)_2$, or heteroaryl;

each R^9 is independently hydrogen, oxo, acyl, hydroxyl, hydroxyalkyl, cyano, halogen, C1 – C6 alkyl, aralkyl, haloalkyl, heteroalkyl, cycloalkyl, heterocyclyl, heterocyclylalkyl, alkoxy, dialkylaminyl, dialkylamidoalkyl, or dialkylaminylalkyl, wherein the C1 – C6 alkyl may be optionally substituted with cycloalkyl;

each R^{10} is independently hydrogen, acyl, C1 – C3 alkyl, heteroalkyl or hydroxyalkyl;

R^{11} is haloalkyl;

R^A is halogen;

m is zero or an integer between 1 and 2.

2. The compound of claim 1, wherein Y is O.

3. The compound of claim 1, wherein R^2 is selected from the group consisting of hydroxyalkyl, alkylaminylalkyl, dialkylaminylalkyl, $-ZNR^5R^{10}$, heterocyclyl and

heterocyclylalkyl, wherein each of the Z, heterocyclyl or heterocyclylalkyl are independently optionally substituted with R^9.

4. The compound of claim 3, wherein the heterocyclyl of the heterocyclylalkyl is independently azetidinyl, methylazetidinyl, ethylazetidinyl, isopropylazetidinyl, difluoroazetidinyl, cyclopentylazetidinyl, tetrahydropyranylazetidinyl, tetrahydropyranyl, pyrrolidinyl, methylpyrrolidinyl, dimethylpyrrolidinyl, isopropylpyrrolidinyl, cycloalkylalkylpyrrolidinyl, hydroxypyrrolindinyl, fluoropyrrolidinyl, difluoropyrrolidinyl, (N-methyl)fluoropyrrolidinyl, (N-methyl)difluoropyrrolidinyl, methoxyethylpyrrolidinyl, (N-methyl)methoxypyrrolidinyl, piperazinyl, dimethylaminylpyrrolidinyl, morpholinyl, methylmorpholinyl, ethylmorpholinyl, isopropylmorpholinyl, oxetanyl, 1,4-oxazepanyl, piperdinyl, methylpiperidinyl acylpiperdinyl, cyanopiperdinyl, cycloalkylpiperdinyl, halopiperdinyl, dihalopiperdinyl, fluoropiperdinyl, difluoropiperdinyl, alkoxypiperdinyl, pyrrolidonyl, thiomorpholinyl-1,1-dioxide, 3-azabicyclo[3.1.0]hexanyl, oxa-5-azabicyclo[2.2.1]heptan-5-yl, or azabicyclo[2.2.1]heptan-2-yl.

5. The compound of claim 4, wherein the (N-methyl)difluoropyrrolidinyl is 3,3-difluoro-1-methylpyrrolidinyl.

6. The compound of claim 4, wherein the heterocyclyl is N-methylpyrrolidinyl.

7. The compound of claim 3, wherein R^2 is dialkylaminylalkyl optionally substituted with one or more R^9.

8. The compound of claim 1, wherein R^4 is aryl optionally substituted with one or more R^7.

9. The compound of claim 8, wherein the aryl is selected from the group consisting of phenyl and naphthyl optionally substituted with one or more R^7.

10. The compound of claim 9, wherein the phenyl and the naphthyl are each optionally substituted with one or more R^7 selected from the group consisting of cyano, halogen, hydroxyl, C1- C6 alkyl, hydroxyalkyl, Q-haloalkyl, cycloalkyl, and alkoxy.

11. The compound of claim 1, wherein R^7 is selected from the group consisting of chloro, fluoro, bromo, hydroxymethyl, methyl, ethyl, isopropyl, methoxy, trifluoromethyl, hydroxyl, cyclopropyl and cyano.

12. The compound of claim 1, wherein m is zero.

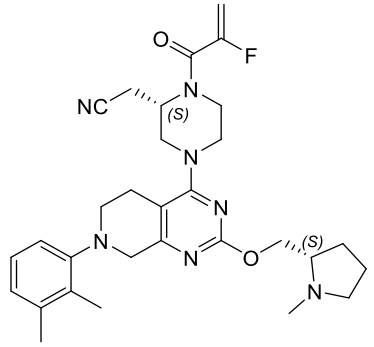
13. The compound of claim 1, wherein L is a bond.

14. The compound of claim 1, wherein R^8 is heteroalkyl, C2-C4 alkynyl, or C1 – C3alkyl optionally substituted with halogen, -OR^5, cyano or heteroaryl.

15. The compound of claim 14, wherein R^8 is C1 – C3 alkyl optionally substituted with cyano.

16. The compound of claim 14, wherein R^8 is cyanomethyl.

17. The compound of claim 1, wherein the compound is:



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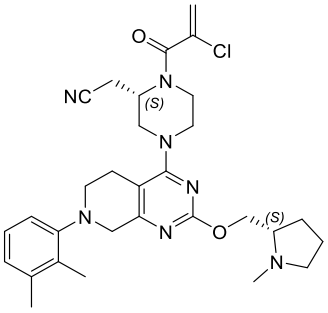

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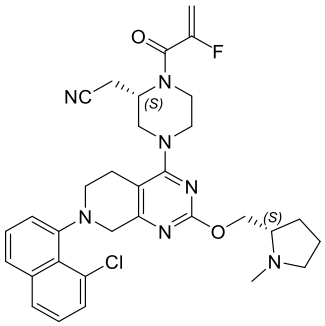

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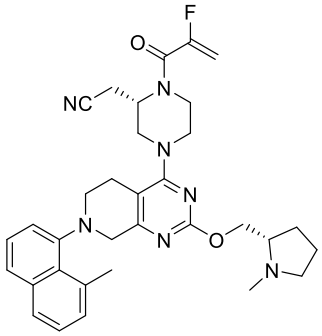

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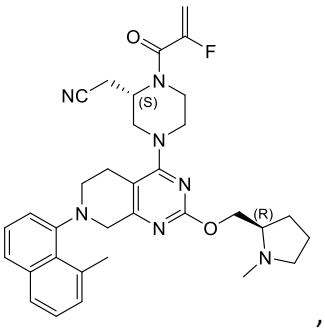
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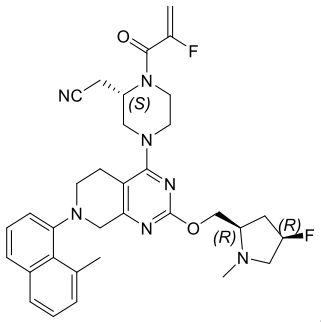
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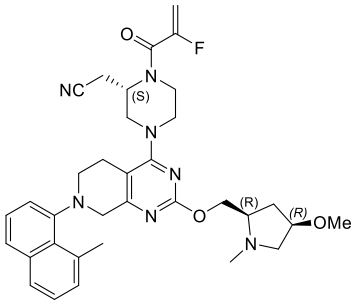
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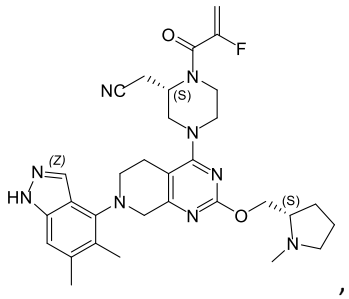
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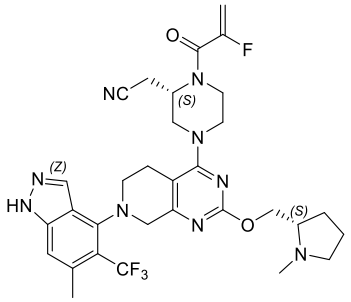
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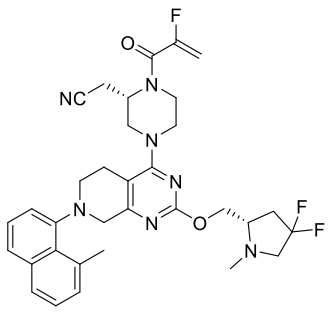
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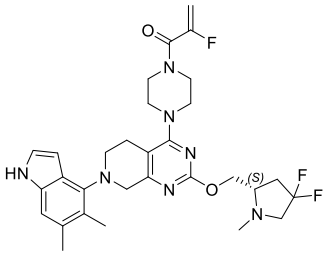
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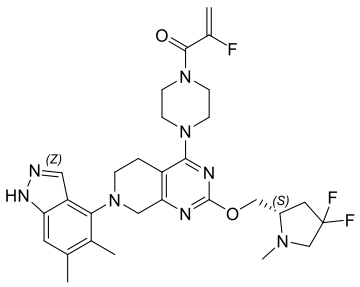
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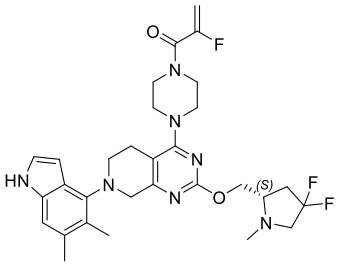
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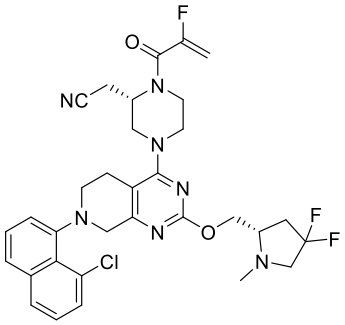
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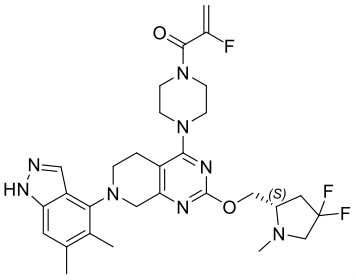
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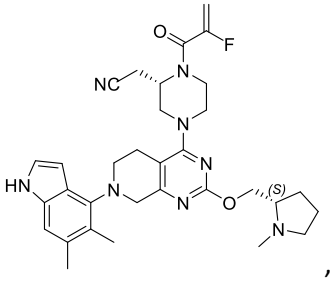
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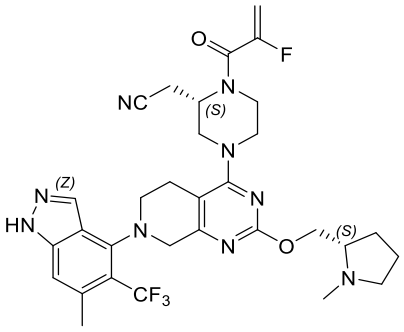
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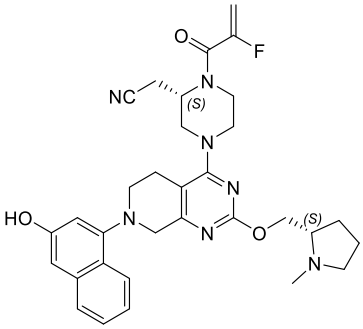
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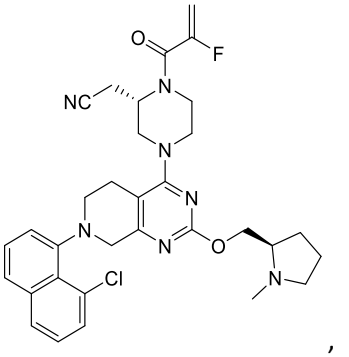
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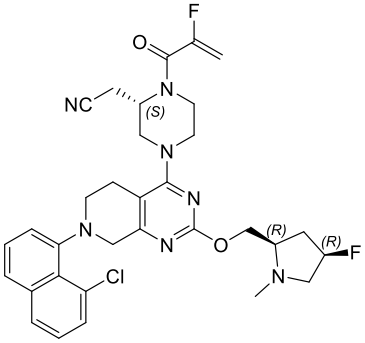
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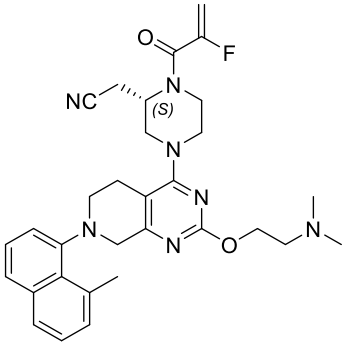
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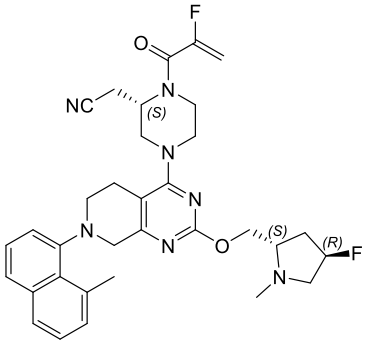
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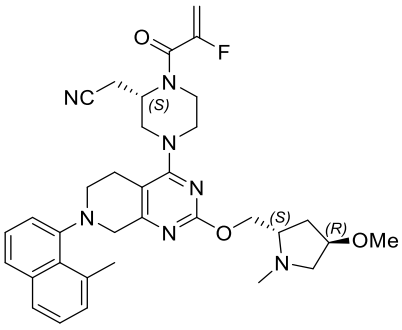
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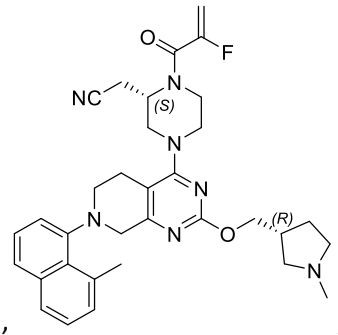
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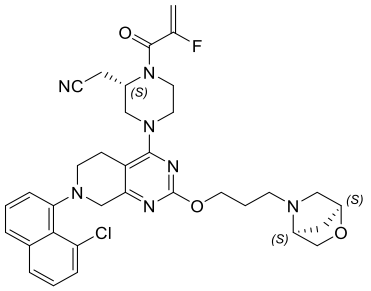
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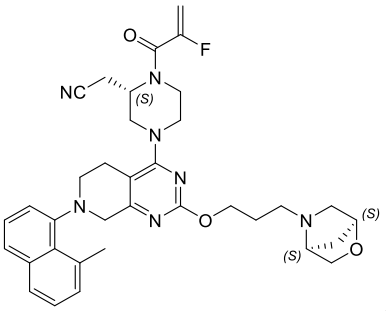
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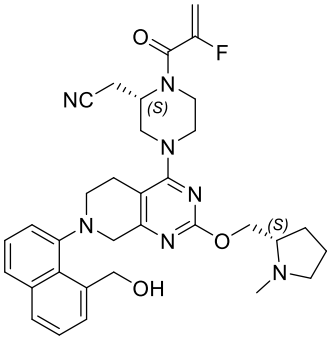
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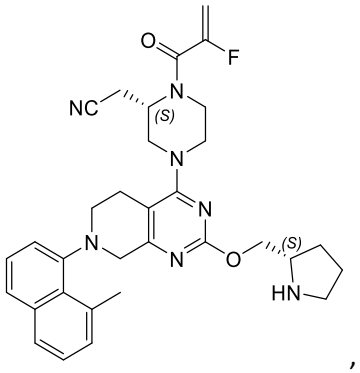
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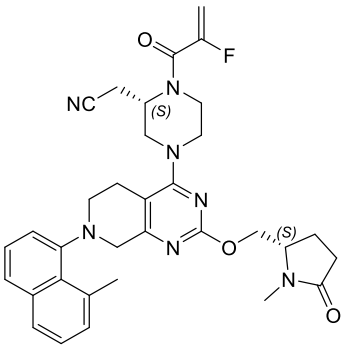
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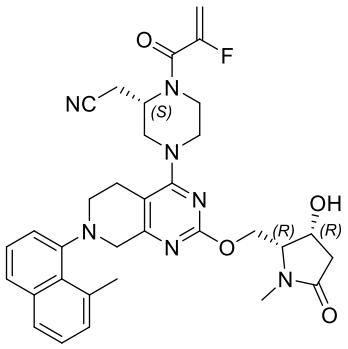
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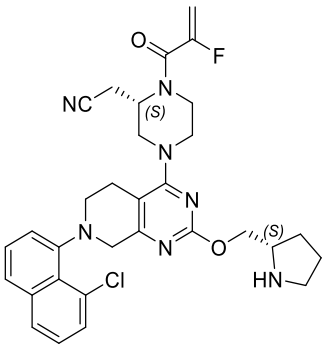
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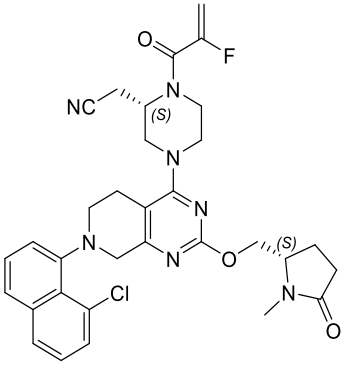
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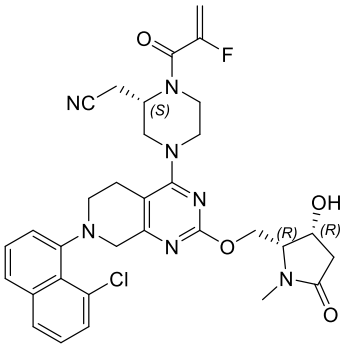
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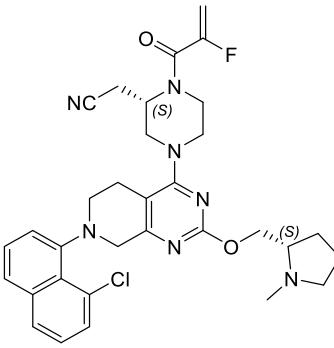
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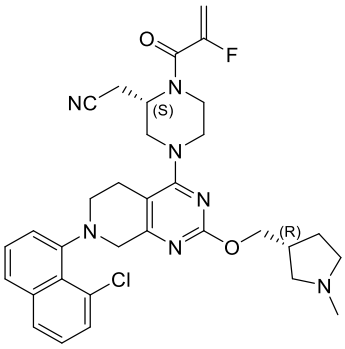
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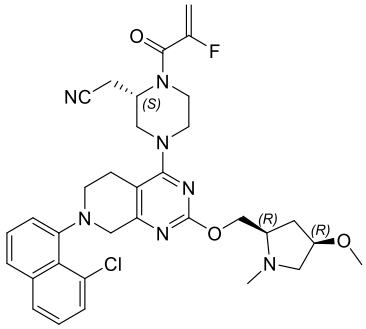
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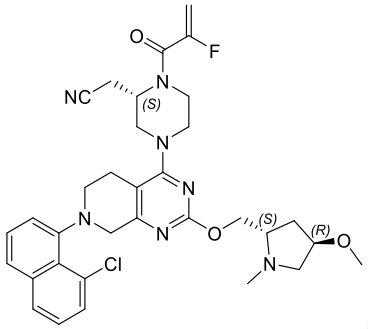
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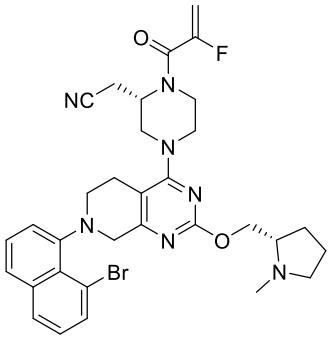
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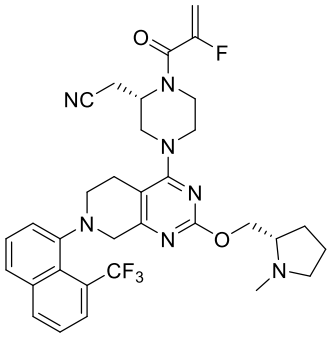
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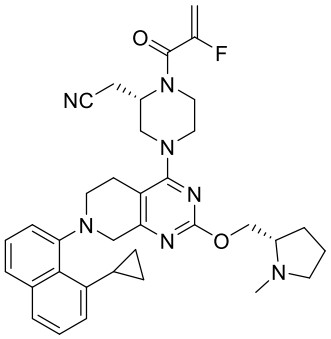
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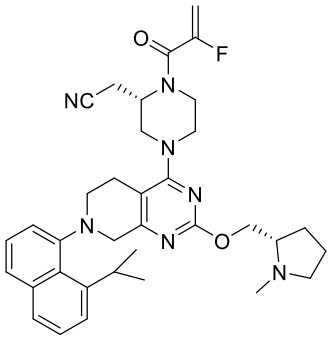
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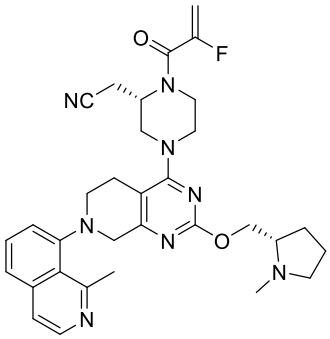
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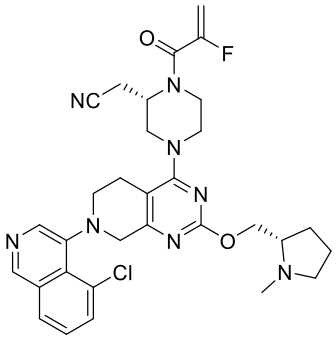
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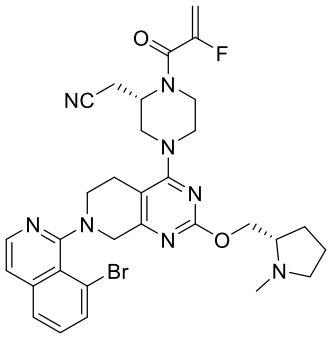
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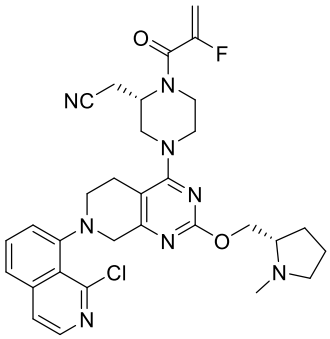
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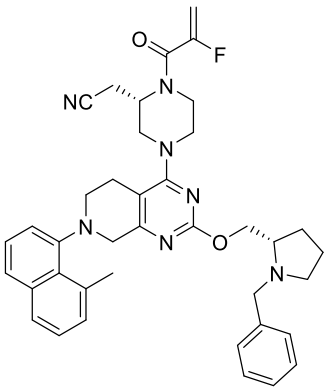
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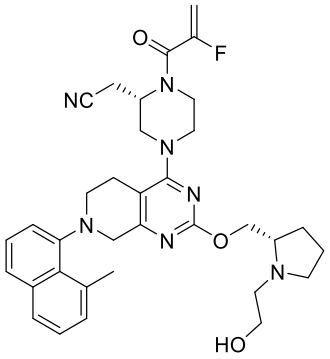
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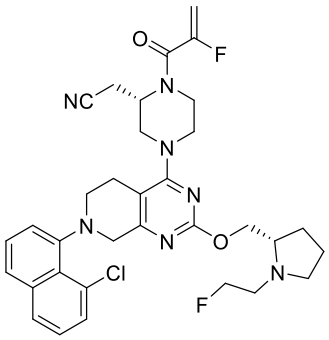
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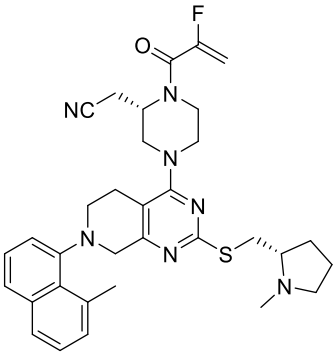
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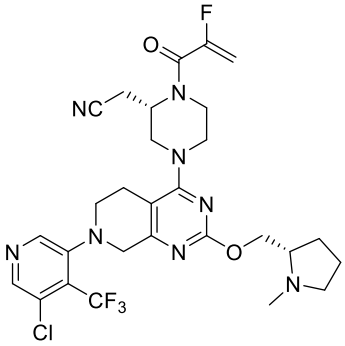
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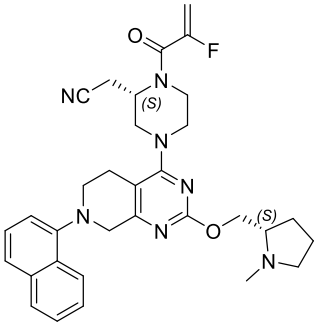
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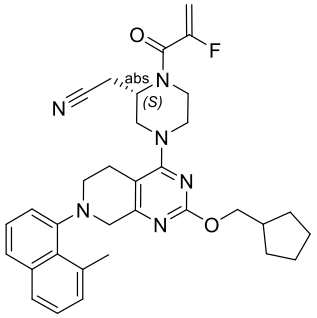
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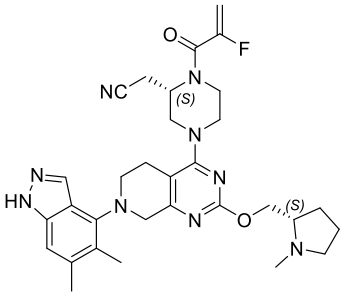
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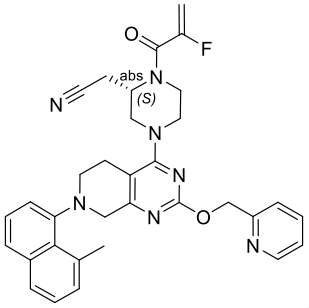
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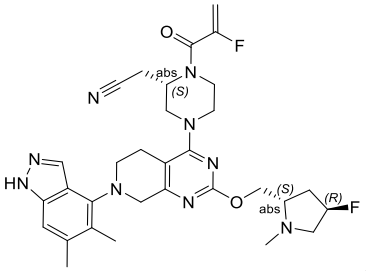
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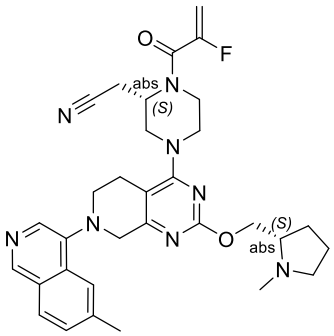
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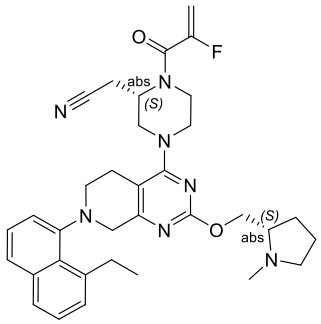
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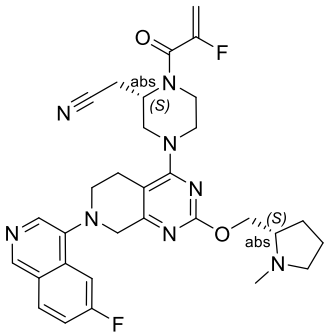
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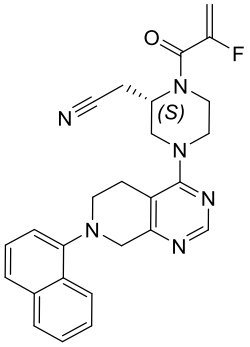
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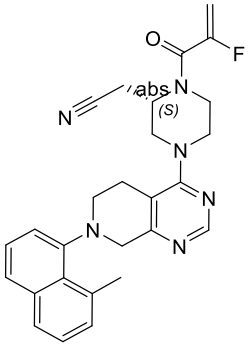
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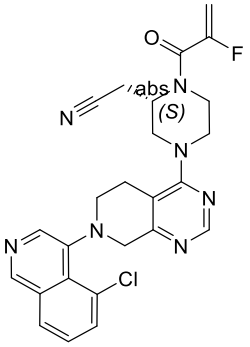
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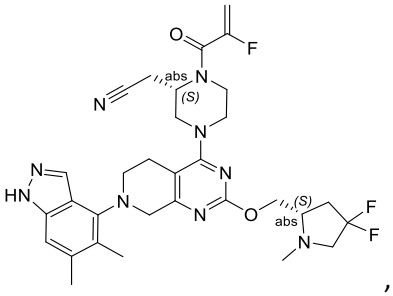
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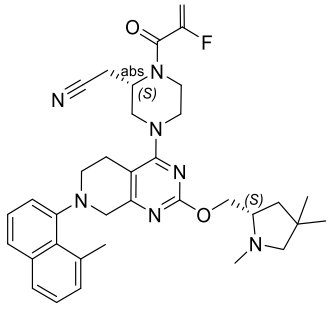
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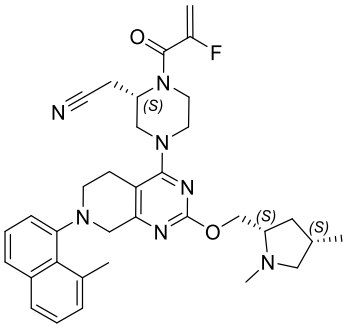
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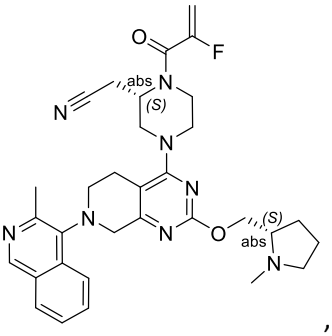
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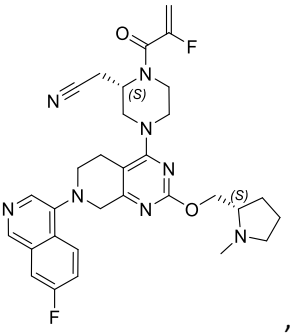
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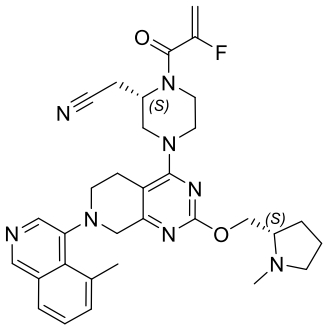
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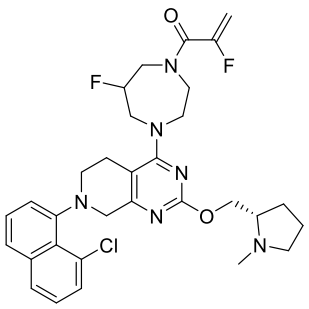
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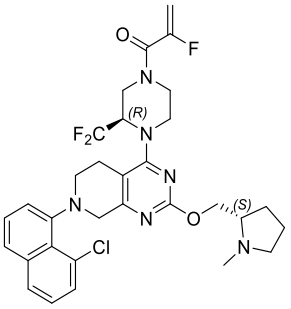
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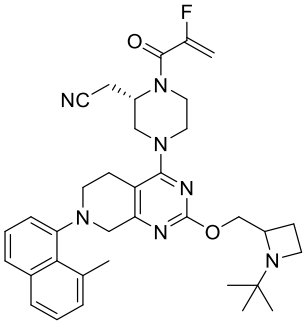
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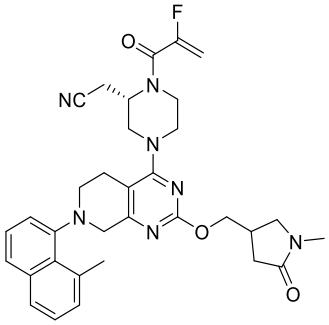
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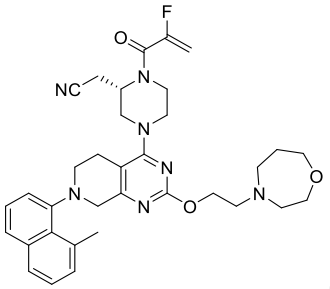
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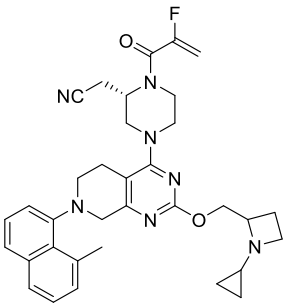
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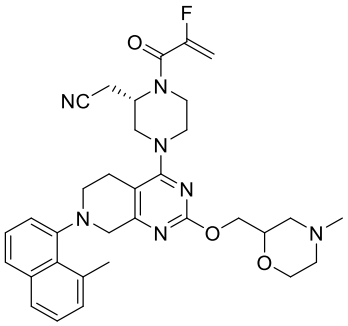
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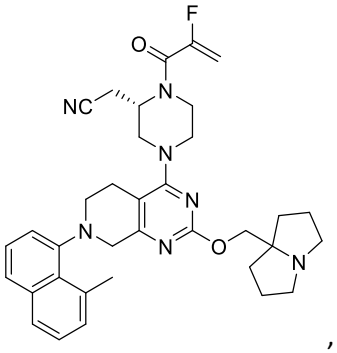
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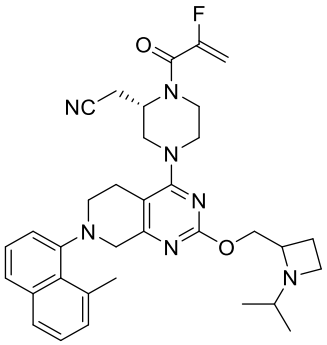
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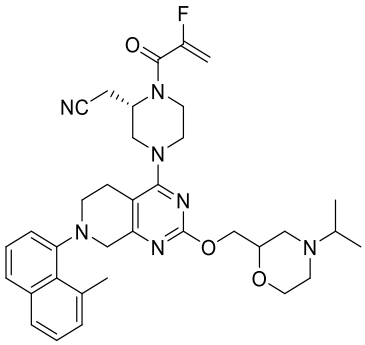
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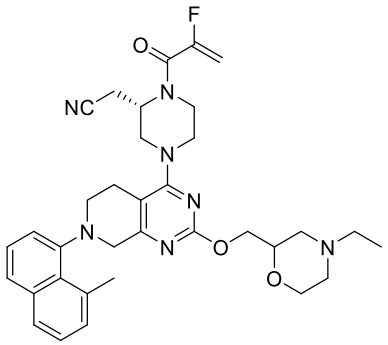
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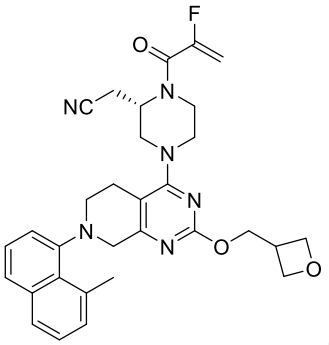
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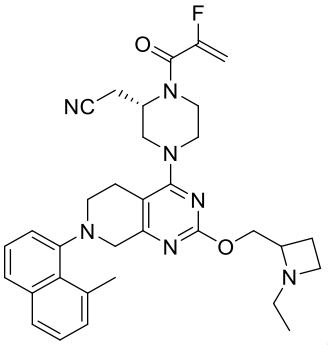
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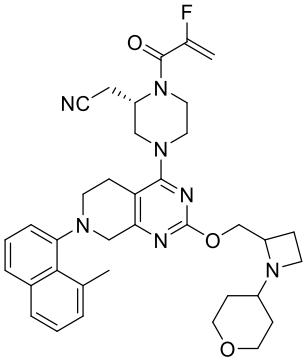
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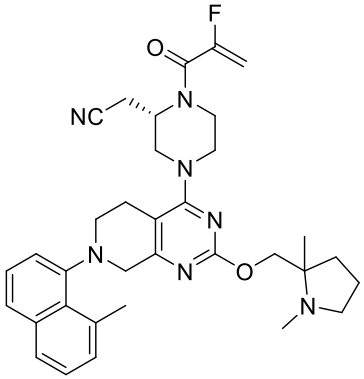
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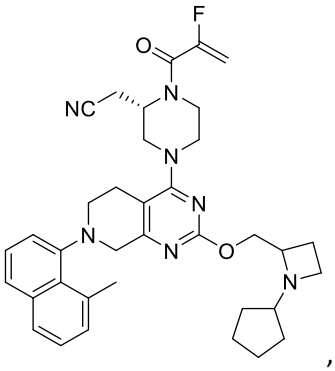
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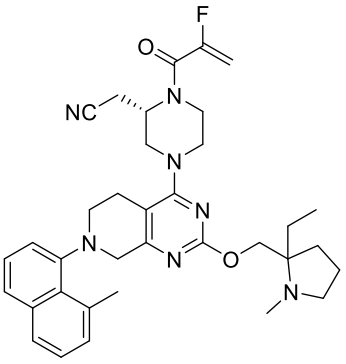
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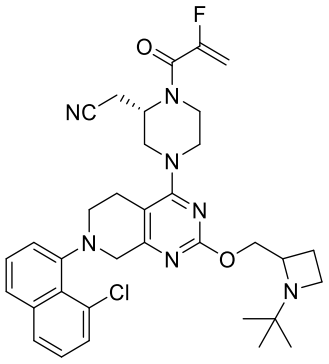
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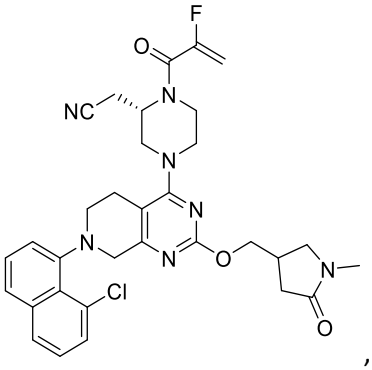
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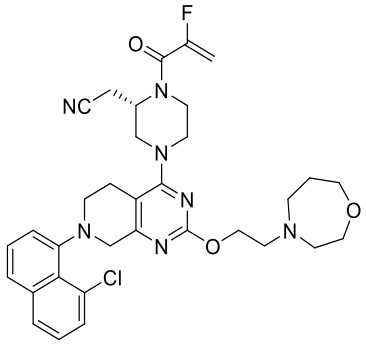
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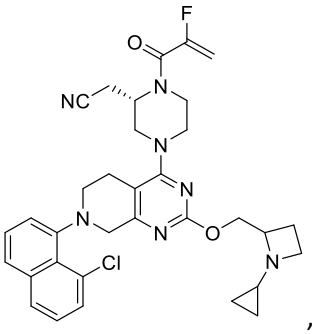
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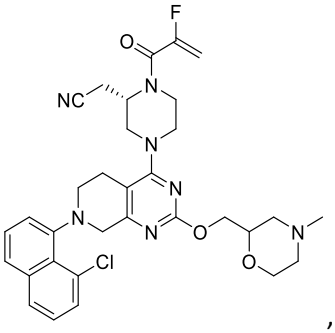
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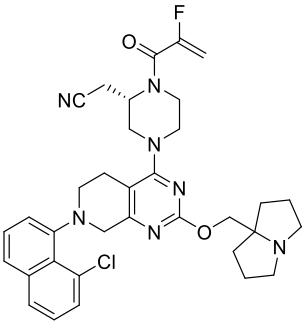
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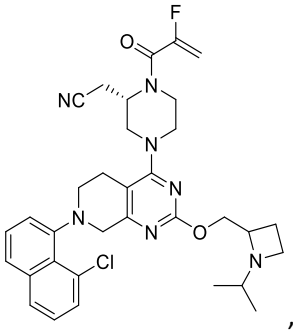
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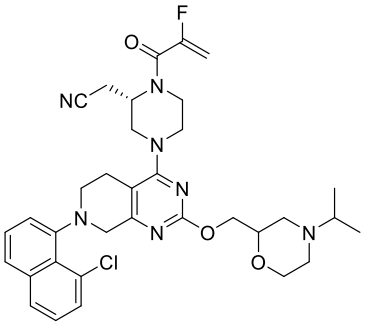
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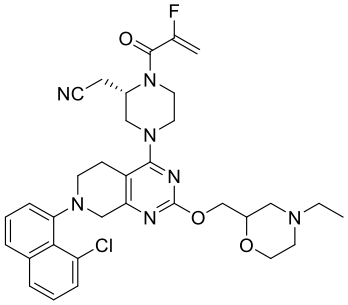
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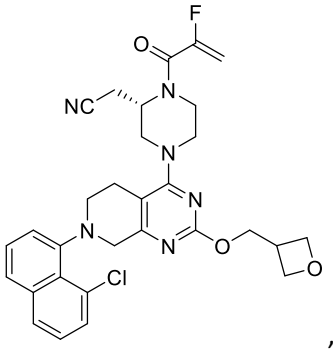
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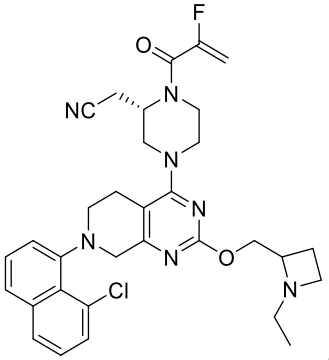
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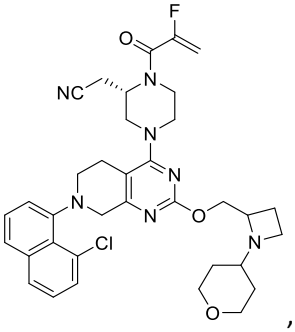
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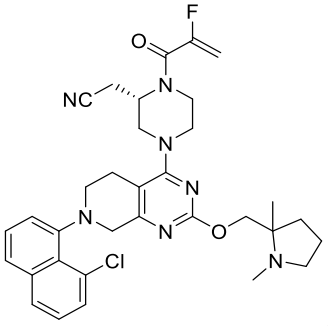
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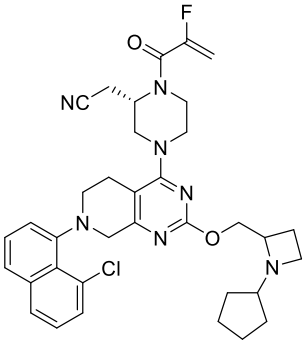
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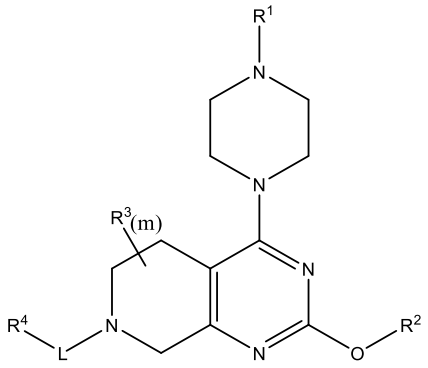
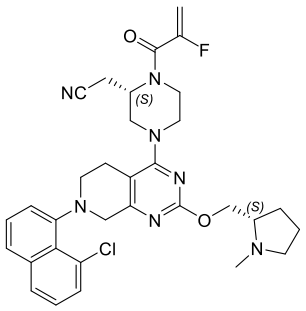
18. The compound of claim 1, wherein the compound is of Formula II-B:



Formula II-B

where the piperazinyl ring is optionally substituted with R^8, and R^1, R^3, R^4, R^8, L and m are as defined in claim 1.

19. A compound of the following structure:



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20. A pharmaceutical composition, comprising a therapeutically effective amount of a compound of Formula (II) according to claim 1, and a pharmaceutically acceptable excipient.

21. An *in vitro* method for inhibiting KRas G12C activity in a cell, comprising contacting the cell in which inhibition of KRas G12C activity is desired with an effective amount of a compound of Formula (II) according to claim 1, pharmaceutically acceptable salts thereof or

pharmaceutical compositions containing the compound of Formula (II), or pharmaceutically acceptable salt thereof.

22. Use of a therapeutically effective amount of a compound of Formula (II) or a pharmaceutically acceptable salt thereof according to claim 1, alone or combined with a pharmaceutically acceptable carrier, excipient or diluents in the manufacture of a medicament for treating a KRas G12C-associated cancer in a patient having cancer.

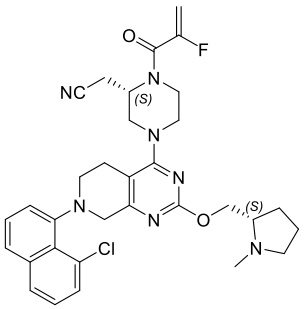
23. The use of claim 22, wherein the therapeutically effective amount of the compound is between about 0.01 to 100 mg/kg per day.

24. The use of claim 22, wherein the cancer is selected from the group consisting of Cardiac: sarcoma , myxoma, rhabdomyoma, fibroma, lipoma and teratoma, wherein the sarcoma comprises angiosarcoma, fibrosarcoma, rhabdomyosarcoma and liposarcoma; Lung: bronchogenic carcinoma , alveolar carcinoma, bronchial adenoma, sarcoma, lymphoma, chondromatous hamartoma, mesothelioma, wherein the bronchogenic carcinoma comprises squamous cell carcinoma, undifferentiated small cell carcinoma, undifferentiated large cell carcinoma and adenocarcinoma, and wherein the alveolar carcinoma comprises bronchiolar carcinoma; Gastrointestinal: esophagus cancer wherein the esophagus cancer comprises squamous cell carcinoma, adenocarcinoma, leiomyosarcoma and lymphoma; stomach cancer wherein the stomach cancer comprises carcinoma, lymphoma and leiomyosarcoma; pancreas cancer wherein the pancreas cancer comprises ductal adenocarcinoma, insulinoma, glucagonoma, gastrinoma, carcinoid tumors and vipoma; small bowel cancer wherein the small bowel cancer comprises adenocarcinoma, lymphoma, carcinoid tumors, Kaposi's sarcoma, leiomyoma, hemangioma, lipoma, neurofibroma and fibroma; large bowel cancer wherein the large bowel cancer comprises adenocarcinoma, tubular adenoma, villous adenoma, hamartoma and leiomyoma; Genitourinary tract: kidney cancer wherein the kidney cancer comprises adenocarcinoma, Wilm's tumor or the equivalent nephroblastoma, lymphoma and leukemia; bladder and urethra cancer wherein the bladder and urethra cancer comprises squamous cell carcinoma, transitional cell carcinoma and adenocarcinoma; prostate cancer wherein the prostate cancer comprises adenocarcinoma and sarcoma; testis cancer wherein the testis cancer comprises seminoma, teratoma, embryonal carcinoma, teratocarcinoma, choriocarcinoma, sarcoma,

interstitial cell carcinoma, fibroma, fibroadenoma, adenomatoid tumors and lipoma; Liver: hepatoma cancer, cholangiocarcinoma, hepatoblastoma, angiosarcoma, hepatocellular adenoma, hemangioma, wherein the hepatoma cancer comprises hepatocellular carcinoma; Biliary tract: gall bladder carcinoma, ampullary carcinoma, cholangiocarcinoma; Bone: osteogenic sarcoma or the equivalent osteosarcoma, fibrosarcoma, malignant fibrous histiocytoma, chondrosarcoma, Ewing's sarcoma, malignant lymphoma or the equivalent reticulum cell sarcoma, multiple myeloma, malignant giant cell tumor chordoma, osteochronfroma or the equivalent osteocartilaginous exostoses, benign chondroma, chondroblastoma, chondromyxofibroma, osteoid osteoma, giant cell tumors and wherein the malignant lymphoma comprises reticulum cell sarcoma; Nervous system: skull cancer wherein the skull cancer comprises osteoma, hemangioma, granuloma, xanthoma and osteitis deformans; meninges cancer wherein the meninges cancer comprises meningioma, meningiosarcoma and gliomatosis; brain cancer wherein the brain cancer comprises astrocytoma, medulloblastoma, glioma, ependymoma, germinoma or the equivalent pinealoma, glioblastoma multiform, oligodendroglioma, schwannoma, retinoblastoma, congenital tumors, spinal cord neurofibroma, meningioma, glioma and sarcoma; Gynecological: uterus cancer wherein the uterus cancer comprises endometrial carcinoma, granulosa-thecal cell tumors, Sertoli-Leydig cell tumors, dysgerminoma and malignant teratoma, wherein the endometrial carcinoma comprises serous cystadenocarcinoma, mucinous cystadenocarcinoma and unclassified carcinoma; vulva cancer wherein the vulva cancer comprises squamous cell carcinoma, intraepithelial carcinoma, adenocarcinoma, fibrosarcoma and melanoma; vagina cancer wherein the vagina cancer comprises clear cell carcinoma, squamous cell carcinoma, botryoid sarcoma or the equivalent embryonal rhabdomyosarcoma and fallopian tubes carcinoma; Hematologic: blood cancer , acute lymphoblastic leukemia, chronic lymphocytic leukemia, myeloproliferative diseases, multiple myeloma, myelodysplastic syndrome, Hodgkin's disease, non-Hodgkin's lymphoma, wherein the blood cancer comprises acute and chronic myeloid leukemia and wherein the non-Hodgkin’s lymphoma comprises malignant lymphoma; Skin: malignant melanoma, basal cell carcinoma, squamous cell carcinoma, Kaposi's sarcoma, moles dysplastic nevi, lipoma, angioma, dermatofibroma, keloids, psoriasis; and Adrenal glands: neuroblastoma.

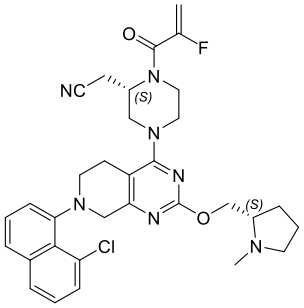
25. The use of claim 24, wherein the cancer is non-small cell lung cancer.

26. A compound of the following structure:



or a pharmaceutically acceptable salt thereof.

27. A pharmaceutically acceptable salt of a compound of the following structure:



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28. Use of a compound or a pharmaceutically acceptable salt thereof according to claim 26 in the manufacture of a medicament for treating non-small cell lung cancer, wherein a patient having non-small cell lung cancer is to be administered with a therapeutically effective amount of said compound or salt, optionally, combined with one or more pharmaceutically acceptable carriers, excipients or diluents.

29. Use of a compound or a pharmaceutically acceptable salt thereof according to claim 26 in the manufacture of a medicament for treating colorectal cancer, wherein a patient having colorectal cancer is to be administered with a therapeutically effective amount of said compound or salt, optionally combined with one or more pharmaceutically acceptable carriers, excipients or diluents.

30. Use of a compound or a pharmaceutically acceptable salt thereof according to claim 26 in the manufacture of a medicament for treating endometrial cancer, wherein a patient having endometrial cancer is to be administered with a therapeutically effective amount of said compound or salt, optionally combined with one or more pharmaceutically acceptable carriers, excipients or diluents.

31. Use of a compound or a pharmaceutically acceptable salt thereof according to claim 26 in the manufacture of a medicament for treating pancreatic cancer, wherein a patient having

pancreatic cancer is to be administered with a therapeutically effective amount of said compound or salt, optionally combined with one or more pharmaceutically acceptable carriers, excipients or diluents.